Differential DNA methylation in bronchial biopsies between persistent asthma and asthma in remission

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Former asthma patients have epigenetic modifications not present in current asthma which are associated with the activity of genes involved in the resolution of inflammation. Their epigenetic profile also shows them to be different from healthy controls. http://bit.ly/2BGmCPl

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ABSTRACT Approximately 40% of asthmatics experience remission of asthma symptoms. A better understanding of biological pathways leading to asthma remission may provide insight into new therapeutic targets for asthma. As an important mechanism of gene regulation, investigation of DNA methylation provides a promising approach. Our objective was to identify differences in epigenome wide DNA methylation levels in bronchial biopsies between subjects with asthma remission and subjects with persistent asthma or healthy controls.

We analysed differential DNA methylation in bronchial biopsies from 26 subjects with persistent asthma, 39 remission subjects and 70 healthy controls, using the limma package. The comb-p tool was used to identify differentially methylated regions. DNA methylation of CpG-sites was associated to expression of nearby genes from the same biopsies to understand function.

Four CpG-sites and 42 regions were differentially methylated between persistent asthma and remission. DNA methylation at two sites was correlated *in cis* with gene expression at *ACKR2* and *DGKQ*. Between remission subjects and healthy controls 1163 CpG-sites and 328 regions were differentially methylated. DNA methylation was associated with expression of a set of genes expressed in ciliated epithelium.

CpGs differentially methylated between remission and persistent asthma identify genetic loci associated with resolution of inflammation and airway responsiveness. Despite the absence of symptoms, remission subjects have a DNA methylation profile that is distinct from that of healthy controls, partly due to

changes in cellular composition, with a higher gene expression signal related to ciliated epithelium in remission *versus* healthy controls.